HORMONE
RESEARCH

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Abstracts

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ing the substitution of Cys 10 by Trp in the NP II moiety . This amino-acid change is expected to destroy a disulfide bridge and to lead to misfolding of the prohormone. When inquired specifically, the mother also reported an abnormal thirst and water consumption. In conclusion, we report a patient with neurohypophyseal diabetes insipidus due to a novel mutation of the AVP-NPII gene. The presenting feature was a longstanding history of failure to thrive and polydipsia in a 5-year-old boy, wrongly considered to have behavioural troubles. The mutation detection in the AVP-NP gene makes the MRI and βhCG follow-up in search of a CNS tumour or hystiocytosis unnecessary.

PO1-632 Neuroendocrinology/Pituitary 1

A novel homozygous D150E mutation in AQP2 gene in a child with nephrogenic diabetes insipidus

Alexey Shandin[1]; Valentina Peterkova[1]; Petr Rubtsov[2]; Anatoly Tiulpakov[1]
[1]Endocrinological Research Center, Institute of Pediatric Endocrinology, Moscow, Russian Federation; [2]Engelhardt Institute of Molecular Biology, Laboratory of Hormones, Moscow, Russian Federation

Aquaporin-2 gene (*AQP2*) encodes a vasopressin-regulated water channel expressed in renal collecting ducts. Mutations in this gene cause autosomal recessive or dominant forms of nephrogenic diabetes insipidus (NDI). We report here a novel homozygous missense mutation in *AQP2* gene in a boy with NDI. A boy from a consanguineous family presented with polydipsia and polyuria in the first months of life. At referral at the age of 9 yr, his urine volume ranged from 6 to 10 L/day (7-12 ml/kg/hr). During water deprivation test the urine osmolality rose from 160 to 614 mOsm/kg H2O, while plasma osmolality remained normal. There was no changes in urine osmolality after a single dose of oral DDAVP (Minirin 0,1 mg). PCR and subsequent direct sequencing of exons and exon-intron boundaries of *AQP2* gene revealed a homozygous missense mutation in exon 2 leading to a substitution of Aspartic Acid to Glutamic Acid at position 150 (D150E). His unaffected mother was heterozygous for this mutation. D150 is a conserved residue located in the second intacellular loop of aquaporin-2. In conclusion, we identified a novel homozygous missense mutation (D150E) in the *AQP2* gene in a patient with NDI and partially preserved urine concentration function.

PO2-633 Neuroendocrinology/Pituitary 2

High rates of early relapses after complete resection and early tumor progressions after incomplete resection of childhood craniopharyngioma - Update after four years of prospective evaluation in "Kraniopharyngeom 2000"

Ursel Gebhardt[1]; Fabian Pohl[2]; Chrissi Kalentzi[3]; Reinhard Kolb[1]; Sabine Schröder[1]; Angela Emser[4]; Niels Sörensen[5]; Hermann L. Müller[1]
[1]Klinikum Oldenburg gGmbH, Department of Pediatrics, Oldenburg, Germany; [2]University Hospital, Department of Radiooncology, Regensburg, Germany; [3]Marienhospital, Department of Pediatrics, Papenburg, Germany; [4]University Mainz, Institute for Medical Biometry, Epidemiology and I, Mainz, Germany; [5]University Hospital, Department of Pediatric Neurosurgery, Würzburg, Germany

In our multicenter cross-sectional study Hit-Endo we collected data on therapy and outcome of 306 patients with childhood craniopharyngioma (CP). The survival rates were 94±4% in irradiated and 93±5% in non-irradiated patients. The German multicenter prospective study Kraniopharyngeom 2000 (www.kraniopharyngeom.de) was initiated in order to collect data on incidence and time course of relapses after complete surgery and tumor progressions after incomplete resection. Furthermore, the impact of irradiation (XRT) on relapse and recurrence rates was analyzed. Since 2001 ninety-six patients with newly diagnosed CP were recruited.. With a high degree of completeness (80-90%) data on neurosurgery, neuroradiology and XRT could be collected prospectively. Complete resection was achieved in 43%, subtotal resection in 45%. XRT was performed in 22 of 96 CP patients; in 18% immediately after subtotal resection, in 53% after progression of residual tumour and in 14% after (second surgery of) relapse. Data on XRT modalities were evaluable in 17 of 22 patients. XRT was performed at a median age of 11 years (4 - 18 y) and after a mean interval of 10 months after first diagnosis. All patients got a 3-dimensional CT-planning of XRT. The mean total dose was 52.5 Gray. An interim evaluation on event-free survival rates (EFS) after four years of patients' recruitment showed a high rate of early events in terms of tumour progression after subtotal resection (EFS: 0.083±0.077) and relapses after complete resection (EFS: 0.63±0.13) during the first three years of follow-up. A high rate of early events (EFS: 0.68±0.13) was also found for patients after XRT. We conclude that progression after subtotal resection and relapse after complete resection of CP are frequent and early events even in irradiated patients during the first three years after diagnosis. Regular monitoring of cerebral imaging and clinical status is recommended in follow-up of patients with CP.

PO2-634 Neuroendocrinology/Pituitary 2

Increasing safety and sensitivity of insulin hypoglycaemia testing; effects of insulin dose and glucometer "cut-offs"

Emma Webb; Mariette Nortier; Helen Spoudeas
University College Hospitals, London, London Centre for Paediatric Endocrinology, London, United Kingdom

The insulin hypoglycaemia test (ITT) is the gold standard for assessing growth hormone (GH) and ACTH reserve but relies on inducing and reversing potentially dangerous, hypoglycaemia. Prior audits in our unit suggested glucometers over-read by 0.5mM, and had only 75% sensitivity for hypoglycaemia (glucometer ≤2.6mM). Almost all (95%) patients achieved hypoglycaemia by 20mins after iv insulin injection, but this went undetected in 20%. We aimed to assess potential improvements in safety and sensitivity of the ITT by: 1. Using a higher glucometer "cut-off" (≤3.0mM) for reversing hypoglycaemia 2. Using a lower dose of i.v. insulin routinely (0.1u/kg) and increasing frequency of glucose monitoring to assess timing and adequacy of hypoglycaemia. Lab glucose and glucometer readings from 24 consecutively booked adolescents aged 13-19 years all given 0.1u/kg i.v. insulin (audit 2) were compared with data from 20 individuals given 0.15u/kg (n9) or 0.1u/kg, (n11) (if hypopituitary) insulin i.v. in a previous audit (1).

	N	Insulin Dose (u/kg)	Glucometer cut-off used (mM)	Mean (SD) lab glucose achieved	N (%) achieving hypoglycaemia by time:			Sensitivity of glucometer at detecting hypoglycaemia at time:		Specificity of glucometer at detecting hypoglycaemia at time:	
					15 mins	20 mins	30 mins	15mins	20 mins	15 mins	20 mins
Audit 1	20	0.15 (0.1 if hypopit)	≤2.6	1.5 (0.3)	Not tested	19 (95%)	20 (100%)	-	79%	-	100%
Audit 2	24	0.1 (all)	≤3.0	1.6 (0.7)	14 (58%)	19 (79%)	22 (92%)	50%	89%	83%	100%

Lower insulin doses increased time to hypoglycaemia (audit 1 vs audit 2; 95% vs 79% at 20mins), but not its level. Glucometer „cut-off" ≤3mM and additional 15min sampling improved earlier detection and sensitivity (audit 1 vs audit 2; 79% vs 89% at 20mins). We conclude that higher glucometer readings (≤3.0mM) should be routinely used. Lower insulin (0.1u/kg) doses may result in 8% „test failure" and reduced specificity. Increased glucose monitoring in combination with routine early reversal (20min) after higher (0.15u/kg) needs assessing.